REMARKS

Applicants take this opportunity to thank Examiner Fox for extending the courtesy of a personal U.S. PTO interview with co-inventor, Dr. Caius Rommens, and Applicants' representative, Dr. Richard Peet, on Tuesday, August 2, 2006. Applicants thank Examiner Fox for his constructive comments at that time and his informative Interview Summary. This paper takes into account those comments and outcome of that interview.

In particular, Applicants acknowledge Examiner Fox's assertion that the amendments discussed during the interview "would overcome" the prior art rejection of the method claims. As Examiner Fox reiterated, and as denoted in the Office Action at page 18, the prior art fails to "teach or reasonably suggest methods of plant transformation which use Agrobacterium but which do not employ T-DNA during the transformation process." Applicants have amended the compositional claims in a similar fashion to make clear that the relevant compositions contain at least a portion of a border-like sequence.

I. Status of the Claims

Claims 3, 5, 13, and 44-57 are pending. Claims 1-2, 4, 6-12, and 14-43 are canceled without prejudice or disclaimer. Applicants reserve the right to file one or more continuing applications to the canceled subject matter. Claims 56 and 57 are withdrawn for allegedly falling outside the scope of the elected restriction Group. Claims 3, 13, 44, 46, and 53 are amended for the following reasons.

(i) Claim 3

Claim 3 is amended simply to make clear that the recited plant cell is transformed "using Agrobacterium," which is consistent with the entire specification's teachings concerning Applicants' novel P-DNA and border-like transformation protocol. In this regard, Applicants also amend claim 3 to make clear that the desired polynucleotide is "flanked by at least one border-like sequence that is not a T-DNA border." This amendment is supported by the entire specification but notably at page 13, paragraph 29. Applicants also amend claim 3 to include the step of "asexually propagating" which is supported by the entire specification, especially paragraphs 0210 and 0240.

(ii) Claim 13

Claim 13 is amended to incorporate Examiner Fox's suggestion to clarify that the progeny plant has the desired polynucleotide in its genome, as recited in claim 3, step (4); and also is amended to make clear that the desired polynucleotide comprises at least a portion of one border-like sequence, wherein that portion does not have a nucleotide sequence that is identical to a portion of a T-DNA. The latter qualification also is recited in claim 3.

These amendments are fully supported by the originally-filed specification. See, for instance, paragraphs 29, 44, 69, 143, and 212, which disclose Applicants' identification and use of border-like sequences and how they are integrated into the plant genome. Paragraph 212 explains that border-like sequences, like conventional T-DNA left and right borders, can function as recognition sites for *virD2*-catalyzed nicking reactions, which facilitate integration of the polynucleotide to which the border-like sequences are attached. As with conventional T-DNA left and right borders, the various nicking enzymes and complexes do not necessarily cleanly cleave the expression cassette at the precise nucleotide junction between a border-like sequence terminus and the desired terminus of the desired polynucleotide. As typically happens, therefore, a part of the left and/or right border is integrated alongside the desired polynucleotide of interest.

(iii) Claims 44 and 46

Claims 44 and 46 are amended simply to replace "transfer DNA" with "carrier DNA" as suggested by Examiner Fox.

(iv) Claim 53

Claim 53 is amended for grammatical reasons to replace "facilitates" with "facilitate."

None of these amendments introduces new subject matter and therefore Applicants respectfully request their entry.

(v) It is unnecessary for the claims to recite a border-like consensus sequence

Applicants thank Examiner Fox for suggesting that Applicants could recite the border-like motif consensus sequence in the claims to further characterize that sequence element and thereby further expedite prosecution. After consideration, Applicants believe that the claims as written, and the detailed guidance provided by the specification, already fully describe what is a "border-like" sequence and that it is unnecessary to actually recite a specific consensus motif sequence.

The specification accurately and clearly teaches methods for (1) identifying and isolating a border-like sequence; such as by (i) searching DNA databases and (ii) employing the polymerase chain reaction (PCR) to identify sequences that satisfy the inventive "border-like" criteria; and (2) testing the functionality of a border-like sequence by infecting an explant with an *Agrobacterium* transformation plasmid that lacks conventional T-DNA borders but which contains one or two border-like sequences and a gene marker expression cassette. If the border-like sequence(s) is functional, in a transformation sense, then the gene marker, such as the neomycin phosphotransferase (*nptII*) gene, will be integrated into the explant genome. In the case of nptII, it will be readily apparent that integration has occurred by the subsequent formation of kanamycin resistant calli.

Applicants also define and describe what is a border-like sequence throughout the specification. See exemplary support at paragraph 0212. Taken together, this disclosure – the identification methods, the functional assay, and the detailed guidance concerning border-like sequences – readily describes the structural and functional characteristics of the claimed "border-like sequence." For more elaborative discussion on the specific consensus sequence, please see Subsections VI and VII below.

Accordingly, Applicants believe that the claims and disclosure negate any requirement to recite particular sequence parameters, such as that defined by the disclosed consensus motif.

II. Status of the Specification

Applicants have amended the various paragraphs of the specification denoted by Examiner Fox as requiring grammatical corrections and clarification of appropriate sequence identifiers. Accordingly, Applicants believe that all of the objections are overcome.

III. Terminal Disclaimers

(i) Claims 3, 5, 14, 44-49 and 51

Examiner Fox indicated in the August 2nd interview that he would withdraw the provisional double-patenting rejection of claims 3, 5, 14, 44-49 and 51 over claims 1-2, 177-189, 192, 195, and 197-198 of USSN 10/369,324.

(ii) Claims 3, 5, 13, and 44-53

Claims 3, 5, 13, and 44-53 are subject to a provisional double-patenting rejection as allegedly unpatentable over claims 1-36 of USSN 10/505,079.

Without acquiescing to this position, and simply to expedite prosecution, Applicants timely file herewith a terminal disclaimer in compliance with 37 C.F.R. 1.321(c)(d), which overcomes this rejection.

IV. Applicants clarify that the progeny plant of claim 13 possesses the desired polynucleotide in its genome and that therefore claim 13 is drawn to statutory subject matter

Claim 13 is rejected under 35 U.S.C. § 101 because it is allegedly drawn to non-statutory subject matter. (Some progeny plants allegedly could lose the desired transgene via Mendelian segregation and therefore be indistinguishable from naturally occurring plants).

Applicants thank Examiner Fox for his suggestion that incorporating into claim 13 the qualification of step (4) of claim 3, namely that the desired polynucleotide in its genome, would obviate this rejection. Applicants have made this amendment and duly request withdrawal of this rejection.

V. Claims 44 and 46 are not indefinite because they recite "carrier DNA"

Claims 44-50 and 54-55 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite because claims 44 and 46 recite "transfer-DNAs and "transfer-DNA," respectively, which is apparently confusing.

Applicants respectfully point out that paragraph 13 of the specification makes clear that "genetic 'expression cassettes,' comprising genes and regulatory elements, are inserted within the borders of *Agrobacterium*-isolated ***transfer DNAs ("T-DNAs")*** and integrated into plant genomes" (emphasis added).

As Examiner Fox correctly points out, however, Applicants also characterize this transfer DNA as a "carrier DNA":

> Carrier DNA: a "carrier DNA" is a DNA segment that is used to carry certain genetic elements and deliver them into a plant cell. In conventional foreign DNA transfer, this carrier DNA is often the T-DNA of Agrobacterium, delineated by border sequences. The carrier DNA described here is obtained from the selected plant species to be modified and contains ends that may be structurally and functionally different from T-DNA borders but shares with such T-DNAs the ability to support both DNA transfer from Agrobacterium to the nuclei of plant cells or certain other eukaryotes and the subsequent integration of this DNA into the genomes of such eukaryotes.

Paragraph 219, page 60.

Examiner Fox says that replacing the objectionable "transfer DNA[s]" term with "carrier DNA[s]" would obviate this rejection. Applicants thank the examiner for this suggestion and, in the interests of expediting prosecution, so amend the claims in question.

VI. The Declaration of co-inventor Dr. Caius Rommens

Before addressing the remaining rejections of record, Applicants take this opportunity to draw Examiner Fox's attention to Dr. Caius Rommens' Declaration under 35 C.F.R. § 1.132, which is appended to this paper. Dr. Rommens, a co-inventor of the present invention, makes clear that the genus of "border-like" elements and plant P-DNAs is (i) fully substantiated by the originally-filed written description support and that (ii) the specification is enabling for plant-derived nucleotide sequences that function as border-like elements, akin to pre-existing Agrobacterium T-DNA border sequences.

Dr. Rommens is the Director of Research & Development at J. R. Simplot Company (Boise, Idaho). Dr. Rommens and his fellow co-inventors have devised a method for genetically engineering a plant without necessarily incorporating foreign DNA, *i.e.*, non-plant DNA, into the plant genome. Specifically, the claimed "all-native" or "all-green" method resolves issues that bacterial and viral genes, that are necessarily present in prior art transformation processes, are undesirable and troublesome because those genes are integrated into the plant genome. One concern is that such non-plant genes could erratically jump from plant to plant or from plant to insect, or to some animal, and thereby confer a trait that is unwanted outside of the original transformation event. Another is that such genes will be harmful when they enter the food chain. This invention solves such problems that have otherwise stymied others in this field.

To elaborate, the claimed method requires transforming a plant by incorporating polynucleotide sequences that are native to the genome of the plant without using *Agrobacterium* T-DNA. In his declaration, Dr. Rommens highlights those portions of the specification that teach how to identify and create the border-like and P-DNA elements that can be used in the claimed method. Please see paragraphs 6 and 12-14 of the Declaration. Specifically, Dr. Rommens teaches methods for isolating operable border-like sequences from any plant species. The specification teaches one may search DNA databases and employ the PCR reaction to identify sequences that function as border-like sequences when transformed via Agrobacterium into tobacco. Dr. Rommens explains how his analysis of numerous border and border-like sequences culminated in the creation of a "border motif" consensus

sequences. Please see paragraph 8 and also Table 2 at page 60 of the specification, which lists border and border-like sequences. The calculated motif sequence comprise a "central core region," and, together, the motifs provide a permutational framework within which to build any border-like sequence. A border-like sequence does not have to contain a specific motif but the motif provides guidance concerning what constitutes a functional border-like sequence. See paragraph 18:

> Hence, we (1) created, from our analysis of numerous border sequences, a border motif sequence; (2) deduced polynucleotide sequences conforming to that consensus; (3) identified endogenous and native sequences that shared significant sequence identity with our deduced sequence, (4) designed PCR primers based on consensus sequences that can be used to isolate functional border-like sequences for any plant species, and (5) identified a central core region that often represents a good predictor for functional activity of the native sequences.

Dr. Rommens also explains that the present specification provides a functional assay for testing the activity of the fabricated sequences. See paragraph 20.

Accordingly, Dr. Rommens explains that the genus of border-like and P-DNA sequences is substantiated by written description support in the originally-filed application. For instance, the genus is supported by (1) the individual sequences of both T-DNA borders and border-like elements from plant genomes, including those from potato, (2) the consensus sequence that Dr. Rommens derived from his analysis of those individual sequences, and (3) methods for identifying operable border-like elements from any plant species found in the specification. Dr. Rommens concludes at paragraph 25 that:

> . . . we do in fact identify and isolate a multitude of P-DNA border sequences. Furthermore, we also do in fact functionally evaluate those exemplified border-like sequences.

The specification clearly provides a detailed description of methods for identifying functional border-like elements from diverse plant species. With this in mind, Applicants now address the remaining rejections of record.

VII. There is written description for the genus of border-like and P-DNA sequences

Claims 3, 5, 13, and 44-55 are rejected under 35 U.S.C. § 112, first paragraph as failing to comply with the written description requirement because, from the examiner's point of view, the specification "only demonstrates the isolation of two P-DNA border sequences from the single plant species of potato, which border sequences are 25 base pairs long, and comprise SEQ ID NOs: 54 and 55." Office action at page 8. The examiner says that "[n]o guidance has been presented for any other 'transfer DNA' of 'native plant genomic sequences' from any other plant species, or any other length, or any variants thereof; or plant transformation therewith." Office action at page 8. Examiner Fox therefore alleges that there is no written description support for the claimed genus of sequences.

Applicants respectfully point out that, actually, the specification *does* provide other sequences to substantiate the genus of border-like and P-DNA sequences. For example, functional border-like sequences from *R. leguminosarum*, *T. tengcongensis* and *A. thaliana* are described in SEQ ID NOS. 48, 49 and 50, respectively.

Hence, the specification teaches more than just the specific potato sequences denoted by SEQ ID NOs. 54 and 55. Indeed, the specification relates a consensus motif to which a border-like sequence may comport. Thus, the consensus sequence itself inherently describes a multitude of sequences that meet the requirements for the border-like genus. The consensus sequence motif meets the standard set in *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.* 18 USPQ 2d 1016, 1021, namely because the consensus does indeed define the sequence of each species by "its physical or chemical properties." See SEQ ID NO. 47 "Border motif" in Table 2. The sequence is YGRYAGGATATATWSNVBKGTAAWY, where Y= C or T; R= A or G; K= G or T; M= A or C; W= A or T; S= C or G; V= A, C, or G; B= C, G, or T.

In addition, the specification provides a detailed description of methods for identifying functional border-like elements from diverse plant species. Applicants provide detailed methods for identifying and isolating border-like sequences. The specification discloses that one may (1) search DNA databases and (2) employ the polymerase chain reaction (PCR) to identify sequences and actual DNA molecules that satisfy the inventive "border-like" criteria.

Please see Dr. Rommens' Declaration; in particular paragraphs 9, 12-15, and 19-23. In his Declaration, Dr. Rommens testifies that he implemented the methods disclosed in the specification and successfully identified an additional forty-one new border-like sequences. See also Rommens *et al.*, "*Plant-derived transfer DNAs*," *Plant Physiol.* 139: 1338-49, 2005 (appended to the Declaration as Exhibit 2).

Accordingly, Applicants believe that the specification does provide written description of the genus of claimed sequences by virtue of (1) the actual discreet sequences related in the specification, (2) consensus sequences that provide guidance for nucleotide sequence parameters for each species of the genus, and (3) the detailed description of methods for identifying functional border-like elements from diverse plant species found in the specification.

VIII. The specification is enabling for the genus of border-like and P-DNA sequences

Claims 3, 5, 13, and 44-55 are rejected under 35 U.S.C. § 112, first paragraph because allegedly the specification "does not reasonably provide enablement for claims broadly drawn to the use of any plant polynucleotide of any length and sequence for the transformation of any plant species." Office action at page 10.

Applicants would like to first clarify that the recited *desired polynucleotide* contains sequences "that are native to the genome of the plant cell." For instance, the desired polynucleotide may comprise a plant gene of interest operably linked to a plant promoter and a plant terminator, where all three sequences are natural, or "native," to a plant genome. That mini-expression cassette may in turn be flanked by border-like sequences that also are native to a plant genome; or it may be cloned into a plant P-DNA, which necessarily will comprise one or more border-like elements that facilitate transformation. Accordingly, the recited phrase "native to the genome of the plant cell" does not only modify the border-like elements of the entire cassette, but also modifies the desired polynucleotide. Hence, the sequences within the desired polynucleotide, as well as the sequences that facilitate transformation, can be native to the genome of a plant cell.

With that in mind, Applicants turn to the allegations that the specification is not enabling for anything other than the two denoted potato border-like sequences; and that "[P]lant transformation with plant-derived 'border-like' sequences in unpredictable." Office action at page 11.

Applicants actually provide detailed methods for identifying and isolating border-like sequences. Specifically, the specification discloses that one may (1) search DNA databases and (2) employ the polymerase chain reaction (PCR) to identify sequences and actual DNA molecules that satisfy the inventive "border-like" criteria. Please see Dr. Rommens' Declaration, paragraphs 9 and 19-23. There, Dr. Rommens testifies that he implemented the methods disclosed in the specification and successfully identified an additional forty-one new border-like sequences. See also Rommens *et al.*, "*Plant-derived transfer DNAs*," *Plant Physiol.* 139: 1338-49, 2005 (appended to the Declaration as Exhibit 2).

The specification also teaches a method for testing the functionality of a newly-identified border-like sequence. Applicants performed that assay and demonstrated that the potato P-DNA of SEQ ID NO. 1 could successfully transform tobacco. See paragraph 345. The functional assay requires:

(a) inserting the border-like sequence and a neomycin phosphotransferase (*nptII*) gene into a plasmid that lacks T-DNA border sequences, such as pSIM100-OD-IPT; and then introduce that plasmid into an Agrobacterium strain (see paragraphs 31, 341, and 344);

(b) infecting a plant explant, e.g., tobacco, with the Agrobacterium. See paragraph 345; and

(c) identifying the subsequent formation of kanamycin resistant calli. Explants that containing the nptII gene will be kanamycin resistant and therefore identifiable as successfully transformation events. As an aside, the number of individual calli that are identified serves as a general indicator of the transformation efficiency of the border-like element. See paragraph 345 of the specification.

The inventors also used the traditional tobacco model to test the transformation capabilities of numerous border-like sequences that they had identified and isolated from Arabidopsis, potato, tomato, alfalfa, Medicago, barley, Brassica, corn, wheat, and rice. In total, Dr. Rommens attests that he repeated the methods disclosed in the specification exactly for (A) identifying and isolating new border-like sequences and (2) testing the transformation functionality of those sequences. In so doing, Dr. Rommens has isolated over three dozen border-like sequences: 1 from Arabidopsis, 6 from potato, 17 from tomato, 2 from Alfalfa, 1 from Medicago, 3 from barley, 2 from Brassica, 1 corn, 1 wheat, and 3 from rice.

Applicants appreciate that a co-transformation event that employs two T-DNA vectors can yield different transformation results compared to a T-DNA/P-DNA vector combination. Those different results, however, do not negate the predictability of those alternative co-transfer combinations. That is, even though a T-DNA/P-DNA co-transformation event may be "ten-fold" less effective than a T-DNA/T-DNA combination at integrating a desired polynucleotide (paragraph 385 and 389), the T-DNA/P-DNA arrangement still works. Indeed, Applicants' specification teaches how to improve transformation efficiency by selectively enhancing desired integration events. See, for instance, Examples 10-14 of the application.

After reading and implementing the disclosed methods, the skilled person would not be burdened by any undue experimenation. The specification is very clear. The skilled person would have learned (1) how to identify and isolate a border-like sequence; and (2) how to test the functionality of that sequence for plant transformation. The specification therefore provides a very clear, informative, and enabling disclosure for performing each of these three general steps.

IX. All of the claims should be free of the prior art because the Patent Office found no reference that teaches or suggests a method of Agrobacterium-mediated plant transformation that does not employ a T-DNA, as presently recited

Examiner Fox finds that:

> "Claims 44-50 and 54-55 are deemed free of the prior art, given the failure of the prior art to teach or reasonably suggest methods of

plant transformation which use Agrobacterium but which do not employ T-DNA during the transformation process."

Emphasis added; office action at page 18.

Applicants believe that claims 3, 5, 13, and 51-53 should also be free of the prior art, alongside claims 44-50 and 54-55, because the distinguishing qualification (that transformation "does not employ T-DNA") is actually recited in independent claim 3: "wherein the step of transforming the plant cell with the desired polynucleotide does not employ an *Agrobacterium* T-DNA." Furthermore, Applicants make clear in claim 3 that the step of transforming the plant cell is via Agrobacterium-mediated transformation.

According to the Examiner's finding and rationale for judging claims 44-50 and 54-55 to be free of the prior art, claim 3 also should be deemed free of the prior art. Nonetheless, Applicants address the Examiner's anticipatory and obviousness rejections below.

X. McElroy does not anticipate the pending claims because it does not describe an Agrobacterium-mediated transformation method that excludes T-DNAs and also does not teach incorporation of an all-native desired polynucleotide into a plant genome as presently claimed

Claims 3, 5, 13, and 51-52 are rejected under 35 U.S.C. § 102(e) as allegedly anticipated by U.S. Patent No. 6,750,379 ("McElroy"). According to the Examiner, McElroy teaches "the desirability of obtaining transformed plants without the use of T-DNA and wherein selectable marker genes are not integrated into the plant genome." Office action at page 14. McElroy's plants are produced by particle bombardment-mediated transformation.

At the outset, Applicants reiterate that claim 3 should be free of the prior art because Examiner Fox found the prior art failed to teach or reasonably suggest methods of plant transformation which use Agrobacterium but which do not employ T-DNA during the transformation process. Office action at page 18.

Applicants agree with that finding. McElroy says nothing about transforming a plant with an Agrobacterium that *does not* comprise a traditional T-DNA. To the contrary, McElroy only explains that traditional Agrobacterium-mediated transformation is desirable. See col. 42, line 55 to col. 43, line 31. Certainly, McElroy is silent about employing a

nucleotide sequence that resembles a T-DNA left or right border. That is, McElroy says nothing about using "at least one *border-like* sequence" to facilitate transformation and does not contemplate "transforming the plant cell with the desired polynucleotide does not employ an Agrobacterium T-DNA" as recited in claim 3.

McElroy only describes a "method for excision, modification, or amplification of DNA sequences from transgenic cells that does not involve the use of site-specific recombination enzymes," col. 2, line 65 to col. 3, line 2. McElroy's method "instead relies upon directly repeated DNA sequences positioned about the target sequence to direct excision or amplification through native cellular recombination mechanisms," col. 3, lines 3-5. The whole point of McElroy's method is for "excising unwanted DNA sequences from transgenic cells without introducing any further ancillary DNA sequences [e.g., recombinase enzyme gene sequences]." See col. 2, lines 55-57. Hence, McElroy concerns a "direct repeat-mediated homologous recombination" method for plant transformation.

Hence, McElroy does not teach each and every element of the presently claimed invention and therefore does not anticipate claims 3, 5, 13, and 51-52. Applicants therefore respectfully request that this rejection be withdrawn.

XI. No combination of McElroy, Lorberth, and KEYGENE would have motivated the skilled person to modify McElroy in such a way to arrive at the presently claimed invention

Claims 3, 5, 13, and 51-53 are rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over McElroy (*supra*) in view of each of Lorberth, Nature Biotechnology, Vol. 16, pp. 473-477, 1998, and WO 94/03607 ("KEYGENE"). According to the Examiner, McElroy does not "explicitly teach plant transformation with genes-of-interest which down-regulate the R1, PPO, or phosphorylase genes." Office action at page 17. Lorberth, however, apparently teaches transforming a potato plant with an antisense construct that down-regulates R1 expression; while KEYGENE teaches down-regulating polyphenol oxidase also with an antisense construct. Hence, the Office's position is that it would have been obvious to one of ordinary skill in the art to modify McElroy's marker-free, homologous recombination transformation method by "incorporating potato plants as the transformant and

either the R1 or PPO antisense constructs for improvement of starch quality or stored tuber appearance as taught by either Lorberth or KEYGENE." Office action at page 17.

As Applicants related above, the Examiner finds the prior art fails to teach or suggest an Agrobacterium-mediated transformation protocol that does not employ T-DNA. Independent claim 3, however, requires that the step of transforming a plant cell via Agrobacterium-mediated transformation but "does not employ an Agrobacterium T-DNA."

The basis of the obviousness rejection therefore is undercut from the outset. McElroy's method uses site-specific recombination sequences and endogenous enzymes to facilitate cleavage and modification of a sequence positioned between the recombinase recognition sites in a homologous recombination expression cassette. McElroy says only that the "choice of the particular DNA segments to be delivered to the recipient cells will often depend on the purpose of the transformation. One of the major purposes of transformation of crop plants is to add some commercially desirable, agronomically important traits to the plant," col. 18, lines 1-5. Yet, McElroy's method does not concern an Agrobacterium-mediated transformation method that excludes a T-DNA, and certainly does not contemplate an "all-native" transformation approach. McElroy says nothing about using a border-like sequence to facilitate Agrobacterium-mediated plant transformation. Accordingly, McElroy is critically deficient.

Those critical deficiencies are not remedied by either Lorberth or KEYGENE. Lorberth used Agrobacterium-mediated transformation to create a transgenic potato plant that expressed an antisense R1 sequence. Likewise, KEYGENE discloses that "transformed plants can be obtained using standard transformation techniques like Ti-plasmid mediated transformation," as well as by "particle bombardment and the like" for expressing an antisense PPO construct.

Applicants infer that the Office's position is that the person of ordinary skill would have been motivated to substitute one of McElroy's "particular DNA segments" with either Lorberth's R1 antisense construct or KEYGENE's PPO antisense construct. But really the issue is not whether the skilled person would have been motivated to express an antisense

construct for R1 or PPO in McElroy's system; but, rather, whether she would have had any desire for "deleting ancillary sequences, such as selectable marker or reporter genes, from transgenic cells," which is McElroy's fundamental goal (col. 1, lines 14-17). Lorbeth and KEYGENE already had well established methods for expressing their respective antisense constructs in potato plants using traditional Agrobacterium-mediated transformation.

In arguendo, therefore, the person of ordinary skill would have had to have been motivated to (a) down-regulate R1 or PPO and (b) delete any ancillary sequences, such as selectable markers or reporters by using McElroy's homologous recombination method. She would have wanted to express an antisense construct against R1 or PPO but, at the same time, would have necessarily have desired to prevent co-integration of ancillary sequences. Hence, the person of ordinary skill, at the very most, would have been prompted to create a construct in which Lorberth's antisense R1 construct or KEYGENE's antisense PPO construct was positioned between direct repeats of a recombinase enzyme recognition sequence. She would then have proceeded to implement McElroy's method using the modified construct.

Even if the skilled person somehow gleaned that much from the cited references, she would not have been prompted to transform a plant with the McElroy construct using an Agrobacterium vector that lacked a T-DNA. Similarly, she would not have been motivated to ensure that the sequences flanked by the recombinase repeats are native to the plant. The skilled person simply could not have put together any combination of McElroy, Lorberth, and KEYGENE to arrive at the presently claimed invention without hindsight reconstruction, which is impermissible. Nothing in any of the references suggests that it would have been desirable to tinker with McElroy's method to produce the method presently claimed. Accordingly, Applicants assert that for at least these reasons the presently claimed invention is not obvious. Applicants therefore respectfully request withdrawal of this rejection.

XII. Conclusion

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested. The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

Respectfully submitted,

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